

REMARKS

Claim Rejection - 35 U.S.C. § 102

Claims 12-13 and 18 were rejected under 35 U.S.C. 102(b) as being anticipated by Berggren et al. (US 5,620,700). This rejection has been overcome by the cancellation of claims 12-14 and 16-20.

Claim Rejection - 35 U.S.C. § 103

Claims 1-2, 4-6, 8-9, 16, 19, 25-26 and 28-29 were rejected under 35 U.S.C. 103(a) as being unpatentable over Friedman (US 5,002,769) in view of Berggren et al. (US 5,620,700).

Claims 7 and 17 were rejected under 35 U.S.C. 103(a) as being unpatentable over Friedman (US 5,002,769) in view of Berggren et al. (US 5,620,700) as applied to claims 1-2, 4-6 and 8-9 in further view of Miller et al. (US 6,509,031). The rejection is maintained.

Claims 3, 10, 14 and 20 were rejected under 35 U.S.C. 103(a) as being unpatentable over Friedman (US 5,002,769) in view of Berggren et al. (US 5,620,700) as applied to claims 1-2, 4-6, 8-9, 16, 19, 25-26 and 28-29 in further view of Higashi et al. (US 4,906,670).

Looking first at Friedman, column 7, lines 20-23 state that "[w]hen dried to produce the implants of the present invention, such compositions must have a high enough concentration of protein to produce a non-gel-like material having structural stability." (Underlining added).

Thus, Friedman teaches that the dressing must be a non-gel-like material.

Looking now at Berggren, column 4, lines 39-49 read as follows:

The method of the present invention is particularly useful to heat high-viscosity oligomer or polymer formulations so that the viscosity drops in response to heating and softens to produce a flowable, injectable formulation which returns to its higher viscosity upon cooling to the temperature of the biological pocket. The formulation cools to a more viscous consistency with sufficient cohesiveness to be retainable in the biological pocket (possibly with the addition of a biocompatible adhesive), unlike gels or solutions or other fluids. (Underlining added).

Thus, in the biological pocket, the Berggren material is unlike gels.

The Office Action states that "it may be reasonably concluded from the context of the disclosure that the term 'gels' encompass liquid gels and not necessarily more viscous or semisolid to solid gels." The Applicant respectfully disagrees with this conclusion. "[T]he ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005) (en banc). Attached is an excerpt from Remington's Pharmaceutical Sciences - Seventeenth Edition 1985 that states that gels "are characterized by a comparatively high degree of elasticity. They undergo rather large elastic deformations at shear stresses below the yield value, from which they recover their shape when the stresses are removed." Thus, in the pharmaceutical sciences, gels are not liquids as maintained in the Office Action.

It is well settled that in order to establish a *prima facie* case of obviousness of a claimed invention, all of the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). As noted above, Friedman teaches that the dressing must be a non-gel-like material, and Berggren teaches that in the biological pocket, the material is unlike gels. The method of independent claims 1 and 25 requires that "the dressing is a gel at body temperature". Neither Friedman or Berggren teaches this. Therefore, it is submitted that independent claim 1 (and claims 2-10 that depend thereon) and amended independent claim 25 (and claims 26-28 that depend thereon) are patentable over Friedman and Berggren.

Miller was cited as teaching peroxides as a cross-linking agent. It does not make up for the deficiencies of Friedman and Berggren. Higashi was cited disclosing a periodontal disease

treatment comprising atelocollagen and a cross-linking agent. It does not make up for the deficiencies of Friedman and Berggren.

Furthermore, it is well settled that "a prima facie case of obviousness can be rebutted if the applicant ... can show 'that the art in any material respect taught away' from the claimed invention." *In re Geisler*, 116 F.3d 1465, 1469 (Fed. Cir. 1997) citing *In re Malagari*, 499 F.2d 1297, 1303, (CCPA 1974). "A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant," *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir.1994).

As pointed out above, Friedman, at column 7, lines 20-23 state that "[w]hen dried to produce the implants of the present invention, such compositions must have a high enough concentration of protein to produce a non-gel-like material having structural stability." (Underlining added.) Berggren, at column 4, lines 45-49 notes that "[t]he formulation cools to a more viscous consistency with sufficient cohesiveness to be retainable in the biological pocket (possibly with the addition of a biocompatible adhesive), unlike gels or solutions or other fluids. (Underlining added). Given that Friedman teaches that the dressing must be a non-gel-like material, and Berggren teaches that in the biological pocket, the Berggren material is unlike gels, one "would be led in a direction divergent from the path that was taken by the applicant" (i.e., the use of a "dressing [that] is a gel at body temperature" as recited in independent claims 1 and 25). For these reasons, it is also believed that a case of obviousness can be rebutted for independent claim 1 (and claims 2-10 that depend thereon) and amended independent claim 25 (and claims 26-28 that depend thereon) as the "applicant can show 'that the art in any material respect taught away' from the claimed invention."

Conclusion

It is believed that in light of the amendments and arguments presented, the entire application is in condition for allowance.


Because this response has been filed within the statutory period for response, no additional fees are believed due. However, if any other fees are needed, please charge them to Deposit Account 17-0055.

Respectfully submitted,

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Remington's Pharmaceutical Sciences . . . a treatise on the theory and practice of the pharmaceutical sciences, with essential information about pharmaceutical and medicinal agents; also a guide to the professional responsibilities of the pharmacist as the drug-information specialist of the health team . . . A textbook and reference work for pharmacists, physicians, and other practitioners of the pharmaceutical and medical sciences.

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Dilatancy—The opposite behavior, *shear-thickening* or an increase in viscosity with increasing shear, called *dilatancy*,^{2,6-9,12-14} is rare. It is shown by concentrated dispersions of particles which do not tend to aggregate or stick together, provided the amount of liquid present is not much larger than that needed to fill the voids between the particles. Sediments of suspensions from which the supernatant liquid has been decanted are sometimes dilatant. When such a concentrated suspension is poured or stirred slowly, there is just enough liquid to lubricate the slipping of particle past particle, and the viscosity is low. When stirred fast, the particles get into each other's way, block each other and bunch up rather than slipping past each other. Large voids form between the unevenly clustered particles, and as the liquid seeps into these, the suspension appears dry—as if the suspended solids had expanded or become dilated (see sketches in Ref 12 and Ref 14). This phenomenon, which results in progressive viscosity increases, becomes more severe with increasing shear. When high shear is followed by low shear or rest, the bunched-up particles separate again, the interparticle void volume decreases, and the viscosity drops as the suspension appears again wet. Wet sand offers small resistance to slow flow or penetration, but stiffens and appears dry when deformed fast.

Among the few systems reported¹⁴ to exhibit dilatant flow are suspensions of starch in water, aqueous glycerin or ethylene glycol containing about 40–50% *v/v* starch, and concentrated suspensions of inorganic pigments in water and in fluid nonpolar liquids with enough surfactant added to deflocculate the disperse phase completely, e.g., red iron oxide (12% *v/v* in water or 18% *v/v* in carbon tetrachloride), zinc oxide (30% *v/v* in water or 33% *v/v* in carbon tetrachloride), barium sulfate (39% *v/v* in water), and titanium dioxide (30–50% *v/v* in water).

Pseudoplastic and dilatant liquids frequently follow the empirical *power law* (*Ostwald-de Waele equation*)^{1,2,5,6,8,9} over wide ranges of shear rates:

$$\dot{\gamma} = K\tau^n \quad (9)$$

or

$$\log \dot{\gamma} = \log K + n \log \tau \quad (9a)$$

For power-law liquids, a plot of $\log \dot{\gamma}$ vs. $\log \tau$ is a straight line of slope n . This equation has the advantage of representing the flow behavior in terms of only two constants, K and n . It has the disadvantage of all power laws, namely, the dimensions of K depend on the value of n .² Moreover, the power-law curve does not go through the origin, whereas pseudoplastic and dilatant flow curves always do.

The exponent n is an index of the deviation from Newtonian flow behavior. For $n = 1$, $K = 1/\eta$, and Newton's law (Eq 4) results. For pseudoplasticity, $n > 1$ and for dilatancy, $n < 1$. The more n differs from unity, the more non-Newtonian is the flow behavior, ie, the faster will the viscosity decrease or increase with increasing shear.

Yield Value, Elasticity, and Plasticity—Other materials, called semisolids, do not flow at low shear stresses but undergo reversible deformation like elastic solids. When a characteristic shear stress, called the yield value or *yield stress*, is exceeded, they flow like liquids. Yield stresses are usually caused by structural networks extending throughout an entire system. To break such a network requires stresses equal to or exceeding the yield stress. Smaller stresses produce no flow but only elastic deformation. When the yield stress is exceeded, the network is partly ruptured and flow occurs.

There are two classes of semisolid materials with yield stresses, gels and pastes; the distinction between the two is sharp.

Gels—Gels or jellies are characterized by a comparatively

high degree of elasticity. They undergo rather large elastic deformations at shear stresses below the yield value, from which they recover their shape when the stresses are removed.^{6,13} Recoverable deformations of 10–30% are not unusual, especially for polymer gels. Clay gels are less elastic and more like pastes.

Two types of gels are of pharmaceutical importance. *Gels of colloidal clays*, especially of sodium bentonite whose plate-like particles have strong edge-to-face attraction, are discussed first. Their elastic deformability is limited. Their elastic modulus or rigidity and their yield value are not particularly sensitive to changes in temperature. However, the presence of flocculating or deflocculating agents affects these parameters markedly. When subjected to shear stresses well above their yield values, these gels break down to smooth and free-flowing sols.

The second type comprises *aqueous gels of organic polymers* such as gelatin, agar, pectin, methylcellulose, and high-molecular-weight polyethylene glycol. Nonaqueous gels such as natural rubber in benzene are of little pharmaceutical importance.

Solutions of gelatin in water and/or glycerin set to gels on cooling and melt on heating. The gelation temperature and the melting point for a given gel are close together; gelation is a reversible process. Gelatin gels are used in pharmacy as *glycerogelatin*s and as *suppository bases*. The gelation temperature or melting point of gelatin-water systems is in the range of 20–40°. It increases with increasing gelatin content and with increasing gelatin molecular weight, as does the solution viscosity above the gelation temperature and the gel rigidity below it. While the modulus and the ultimate strength of aqueous gels increase with increasing gelatin content, the elongation at break is not much affected.⁵ Gel strength and rigidity are highest at the *isoelectric point*, where cross-linking by salt bridges between amino or guanidino and carboxylate groups is most extensive. While typical aqueous gelatin gels contain 20–45% solids, pectin and agar form strong gels at room temperature which contain only 1–4% solids.

The high viscosity of polymer solutions is largely due to the entanglement of the long, thread-like molecules. The polymer chains are surrounded by a hydration layer, ie, a sheath of water molecules attracted to the polar groups of the macromolecules by secondary valence bonds. Being encased in a solvation sheath largely prevents a polymer chain from forming attachments with neighboring chains at points of entanglement through secondary valence bonds. When the solution is made to flow, the chains slip past one another rather freely and tend to disentangle themselves. If the solvent action decreases, eg, through lowering the temperature or by adding alcohol or another water-miscible nonsolvent to aqueous solutions of gelatin, pectin or agar, the hydration sheath around the dissolved macromolecules becomes thinner. Therefore, some entangled polymer chains come into direct contact with one another at crossover points, where they form attachments by secondary valence bonds. These weak and temporary crosslinks between segments of adjacent polymer chains offer some resistance to the slippage of polymer chains past one another when shear is applied. When enough of these interchain links are formed to establish a three-dimensional network throughout a solution, it sets to a gel. Methylcellulose and high-molecular-weight polyethylene glycol are more soluble in cold than in hot water. They are less extensively hydrated at higher temperatures. Therefore, their solutions gel on heating and melt on cooling.

Polymer gels are strong and elastic. When subjected to shear stresses well in excess of their yield values, they tend to rupture or crumble rather than to flow. Only gels which are weak by virtue of being close to their gelation temperature or of having low solids contents liquefy to sols and flow under the effect of high shear stresses.